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ORIGINAL ARTICLE

Amberlite IRA-400 Cl resin catalyzed synthesis of secondary amines and transformation into *N*-((1*H*-indol-3-yl) (heteroaryl) methyl)-*N*-heteroaryl benzenamines and bis-indoles via multicomponent reaction

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KEYWORDS

Amberlite IRA-400 Cl resin catalyst;
3-Aminoalkylated indole;
Mannich reaction;
Multicomponent reaction;
Amines;
Bis-indole

Abstract A one-pot Amberlite IRA-400 Cl resin catalyzed the *in-situ* generation of imines from various aldehydes and primary amines followed by reduction with sodium borohydride affording corresponding secondary amines. The secondary amines thus obtained were utilized for the IRA-400 Cl resin catalyzed multicomponent synthesis of 3-aminoalkylated indoles using a number of aldehydes and indole. Mild condition, easy work-up, and environmentally benign nature of the synthetic strategy make it both practical and attractive.

1. Introduction

Amines and heterocyclic amine derivatives play a central role as synthons in organic synthesis and are found as the core structure in natural products [1,2], intermediates in fine chemical industries, materials science and biotechnology [3]. One of the most common and practical methods for the preparation of 2° and 3° amines is the direct reductive amination (DRA) of imines generated *in situ* from carbonyl compounds and primary amines followed by reduction with a reducing agent [4,5]. Amberlite resins are heterogeneous catalysts and have been demonstrated to be effective solid catalysts. The commercial Amberlite IRA-400 Cl resin is a divinyl benzene-cross linked gel-type resin where the quaternary ammonium salt of the polystyrene core has been used as a basic catalyst [6–8]. Due to the need for the development of novel environmentally benign synthetic processes, Amberlite IRA-400 Cl resin has emerged as an environmentally benign catalyst for a number

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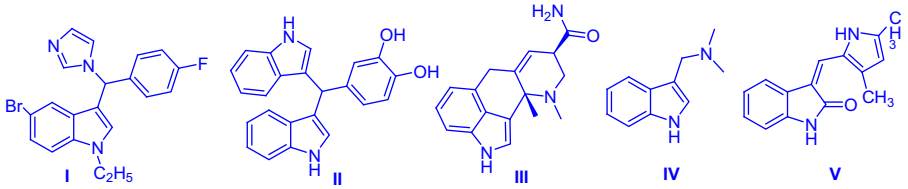
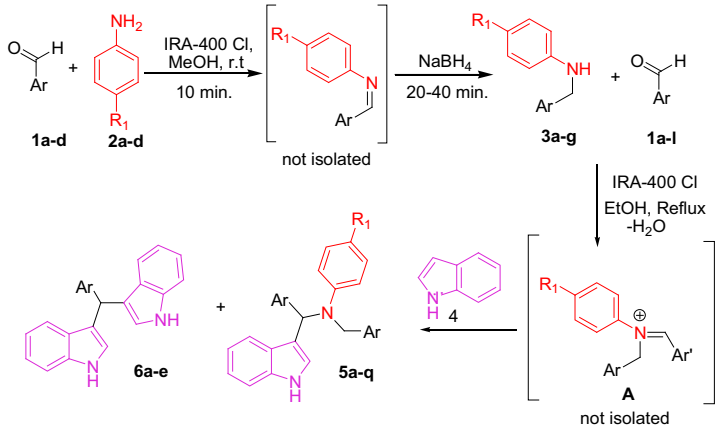


Figure 1 Indole-based bioactive compounds **I–V.**

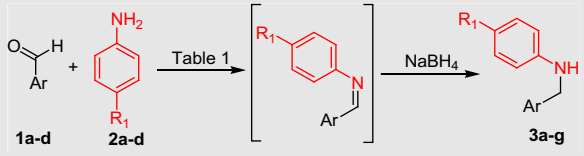


Scheme 1 One-pot synthesis of 3-aminoalkylated indole derivatives.

of synthetic transformations [9–11]. Currently, multicomponent reactions (MCRs) are of interest to chemists as MCRs provide a way for the efficient construction of complex molecules in a one-pot operation without the need to isolate intermediates [12–15]. Indoles with 3-substituent have been considered as venerable pharmacophores in drug discovery and have a wide spectrum of biological applications [16,17], such as 5-HT1B/1D with receptor agonist activity used in the treatment of migraine, aromatase inhibitor for breast cancer **I**, HIV-1 integrase inhibitor **II**, Ergine **III**, Gramine **IV**, and SU5416 **V** is an indole-based FIK-1/KDR inhibitor [18–20] (Fig. 1).

A number of MCR-based synthetic procedures have been developed for the construction of 3-aminoalkylated indoles [21–31]. However, to the best of our knowledge, Amberlite IRA-400 Cl resin catalyzed synthesis of 3-substituted indoles *via* the condensation of *N*-benzyl anilines, aromatic aldehydes, and indole has not been reported. Therefore, herein we report a facile and efficient one-pot synthesis of 3-aminoalkylated indole derivatives involving an MCR methodology catalyzed by Amberlite IRA-400 Cl resin (Scheme 1).

Table 1 Synthesis of amine products **3a–g**.[a]



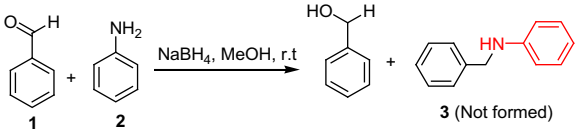
Entry	Ar-CHO 1	Amine (R_1) 2	Time (min.)	Product (Yield %)[b]
1	C_6H_5, **1a**	H, **2a**	30	**3a** (98)
2	4-Cl-C_6H_4, **1e**	H, **2a**	25	**3b** (95)
3	C_4H_4S, **1i**	H, **2a**	40	**3c** (92)
4	C_4H_4O, **1j**	H, **2a**	40	**3d** (90)
5	C_6H_5, **1a**	F, **2b**	30	**3e** (88)
6	C_6H_5, **1a**	Cl, **2c**	30	**3f** (94)
7	C_6H_5, **1a**	OCH_3, **2d**	30	**3g** (92)
8[c]	C_6H_5, **1a**	H, **2a**	30	–

[a] Reaction conditions: aldehyde (**1**) and aniline (**2**), were taken in a 1:1.2 ratio in the presence of 0.5 g of IRA-400 Cl resin in 5 mL of MeOH at r.t.
[b] Isolated yield.
[c] Experiment conducted without IRA-400 Cl resin catalyst.

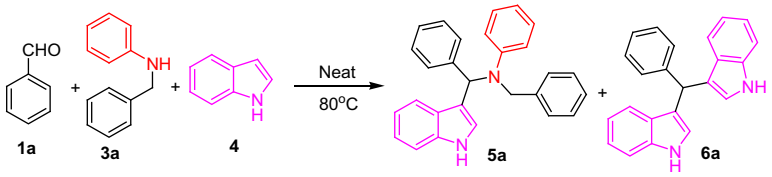
2. Experimental

2.1. General

Fine chemicals used in the reaction were purchased from Spectrochem, SRL and Aldrich Chemical Companies and were used as such without further purification. FT-IR spectra of



Scheme 2 Reductive amination reaction without IRA-400 Cl resin catalyst.



Scheme 3 Synthetic use of the secondary amine **3a**.

Table 2 Optimization of synthesis of **5a**[a].

Entry	Solvent	IRA-400 Cl (mg)	Temp (°C)	Time (h)	Yield (%)[b]	
					5a	6a
1	–	None	80	6	25	48
2	EtOH	500[c]	Reflux	6	10	45
3	MeOH	500	Reflux	6	65	15
4	CH_3CN	500	Reflux	6	70	10
5	$(CH_2Cl)_2$	500	Reflux	6	62	15
6	Toluene	500	Reflux	8	5	25
7	**EtOH**	**500**	**Reflux**	**3**	**85**	**5**
8	EtOH	600	Reflux	3	85	5
9	EtOH	400	Reflux	3	75	10

[a] Reaction conditions: benzaldehyde (**1a**), *N*-benzyl aniline (**3a**), and indole (**4a**) were taken in 1:1.2:1 ratio.
[b] Isolated yield.
[c] Amberlite IR-120 resin was used as catalyst.

Table 3 Recyclability of the Amberlite IRA-400 Cl resin[a] catalyst for the synthesis of **5a**[a].

Entry	Recovery	Time/h	Yield (%)
1	0	3	85
2	1	3	82
3	2	3	80
4	3	3	75

[a] Reaction conditions: benzaldehyde (**1a**), *N*-benzyl aniline (**3a**), and indole (**4a**) were taken in 1:1.2:1 ratio; Amberlite IRA-400 Cl resin[a] (500 mg).

the compounds were recorded on a Thermo Mattson Satellite FT-IR spectrophotometer by the KBr pellet method. The ^1H and ^{13}C NMR spectra were recorded on a Bruker NMR Spectrometer (300.13 and 75.47 MHz/400.13 and 100.6 MHz) or a JEOL-ECA 500 MHz spectrometer (500.13 and 125.77 MHz) using TMS as the internal standard in $CDCl_3$. The following NMR spectra abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and dd = doublet of doublets. Melting points of compounds were determined in open capillaries and are uncorrected. Mass spectra were recorded on a JEOL GCMATE II GC–MS Mass spectrometer. Compound purification was conducted using column chromatography and silica gel. Solvents used for purification are of commercial grade and purified before used. All reactions were carried out under an N_2 atmosphere.

2.2. Procedure for reductive amination of carbonyl compounds: synthesis of *3a-g*

To a solution of carbonyl compounds **1** (2 mmol), amine **2** (2.2 mmol) in reagent grade methanol (4 mL) Amberlite IRA 400-Cl resin (0.5 g) was added. The mixture was vigorously stirred for 10 min at room temperature. Then, $NaBH_4$ (2 mmol) was added in two portions and the mixture was stirred for another 25–40 min. After the completion of the reaction (TLC), the resin was removed by filtration and washed with methanol (2 × 3 mL). The combined organic layer was diluted with EtOAc (15 mL) and washed with water followed by brine. The organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum, and the resulting crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate, 2:1) to afford pure products **3**.

2.3. Spectroscopic data

2.3.1. N-benzyl aniline (*3a*)

Yellow oil; Yield = 98%, FT-IR (KBr): (ν_{max}) = 3375, 3019, 1600, 1495, 1452, 1265, 1172, 1024, 745, 695 cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 4.61 (s, 2H, CH_2), 5.39 (s, 1H, NH), 6.99 (d, J = 7.8 Hz, 2H, Ar-H), 7.16 (t, J = 7.4 Hz, 1H, Ar-H), 7.57–7.62 (m, 2H, Ar-H), 7.66–7.76 (m, 5H, Ar-H); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 48.64, 113.58, 118.12, 127.66, 127.98, 128.95, 129.11, 129.79, 130.66, 140.04, 148.64; Mass (EI) Calcd for $C_{13}H_{13}N$ 183.25; found 183.39.

2.3.2. N-(4-chlorobenzyl) aniline (*3b*)

Yellow oil; Yield = 95%, FT-IR (KBr): (ν_{max}) = 3419, 3057, 2915, 1600, 1501, 1435, 1315, 1260, 1041, 871, 745, 690 cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 4.35 (s, 1H, NH), 4.56 (s, 2H, CH_2), 7.14–7.18 (m, 2H, Ar-H), 7.27 (s, 1H, Ar-H), 7.64–7.66 (m, 2H, Ar-H), 7.84–7.86 (m, 4H, Ar-H); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 46.15, 113.35, 118.12, 127.42, 128.79, 129.34, 129.83 129.92, 133.54,

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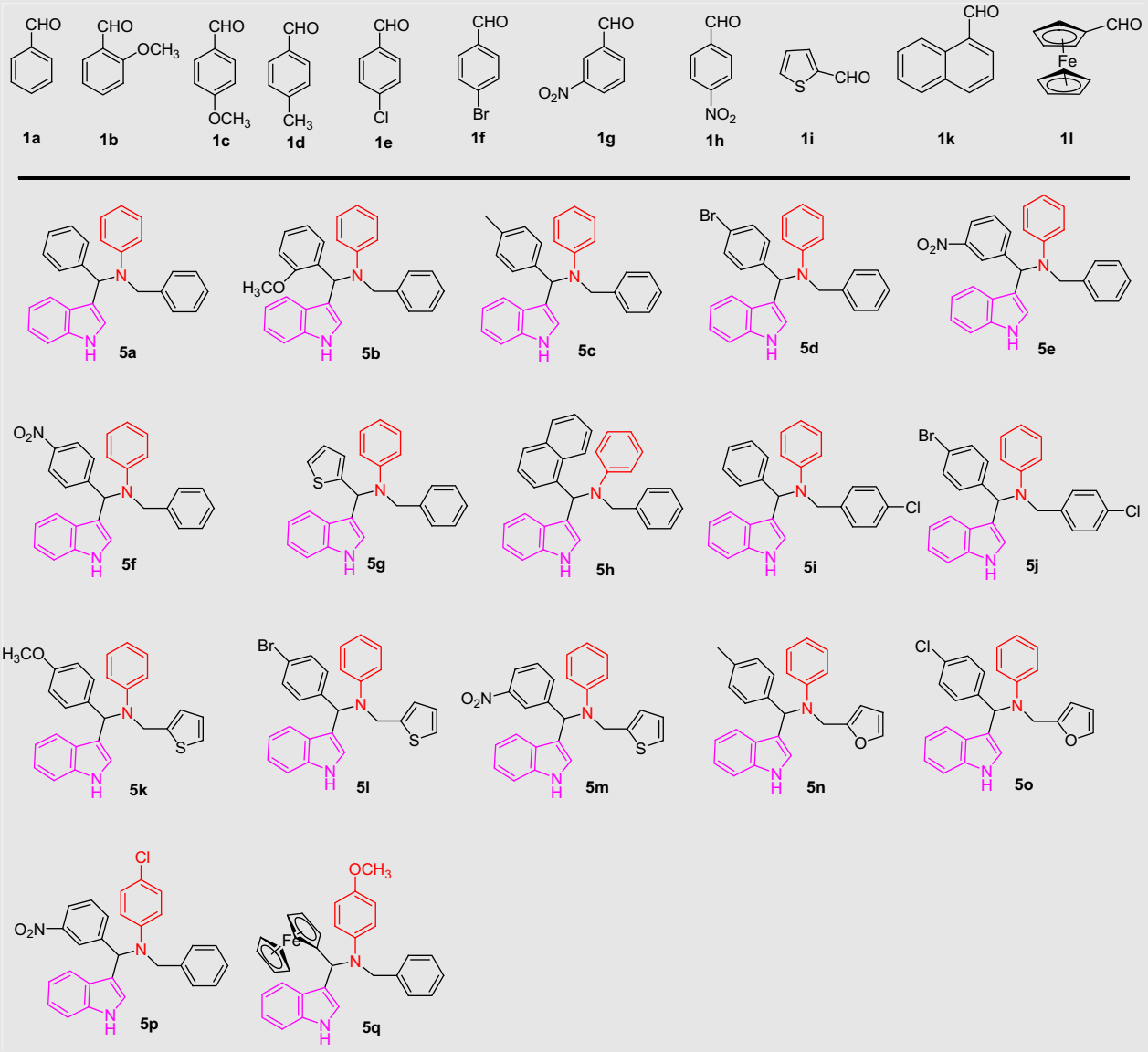
Table 4 Synthesis of 3-substituted indoles catalyzed by Amberlite IRA-400 Cl resin.[a].



Entry	Ar-CHO 1	Amine 3	Indole 4	Time (h)	Product yield (%)
1	**1a**	**3a**	**4a**	2.0	**5a** (85)
2	**1b**	**3a**	**4a**	2.0	**5b** (72)
3	**1d**	**3a**	**4a**	3.0	**5c** (70)
4	**1f**	**3a**	**4a**	2.0	**5d** (74)
5	**1g**	**3a**	**4a**	2.5	**5e** (78)
6	**1h**	**3a**	**4a**	3.0	**5f** (78)
7	**1i**	**3a**	**4a**	3.0	**5g** (70)
8	**1k**	**3a**	**4a**	2.0	**5h** (72)
9	**1a**	**3b**	**4a**	3.0	**5i** (78)
10	**1f**	**3b**	**4a**	2.0	**5j** (75)
11	**1c**	**3c**	**4a**	2.0	**5k** (75)
12	**1f**	**3c**	**4a**	1.5	**5l** (72)
13	**1g**	**3c**	**4a**	3.0	**5m** (72)
14	**1d**	**3d**	**4a**	2.0	**5n** (75)
15	**1e**	**3d**	**4a**	2.0	**5o** (78)
16	**1g**	**3f**	**4a**	2.0	**5p** (80)
17	**1l**	**3g**	**4a**	2.5	**5q** (72)

[a] Reaction conditions: aldehyde (**1**) and aniline (**2**), were taken in a 1:1.2 ratio in the presence of 0.5 g of IRA-400 Cl resin in 5 mL of MeOH at r.t.

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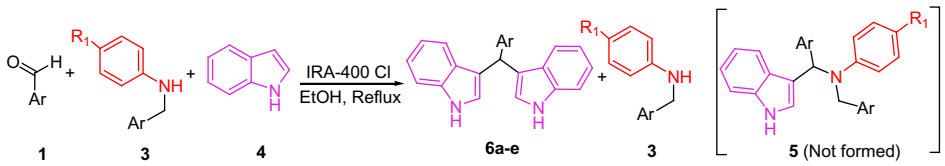


Scheme 4 Limitations and synthesis of bis-indoles.

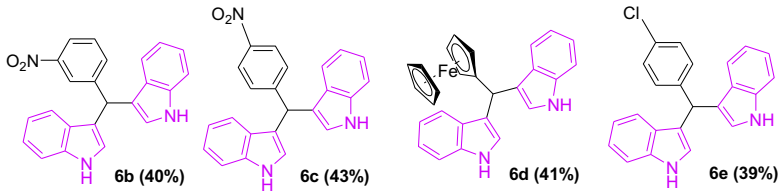
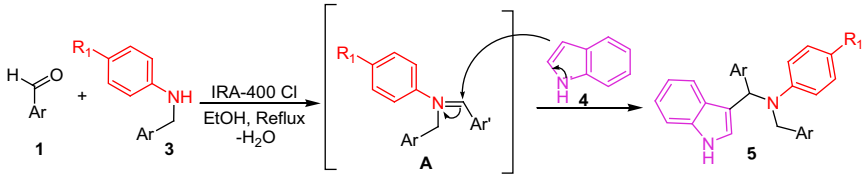


Chart 1 Synthesized bis-indoles.



Scheme 5 Plausible mechanism for the formation of **5.**

Table 5 Synthesis of Bis indole derivatives catalyzed by Amberlite IRA-400 Cl resin.

Entry	Aldehydes	Amines	Indole	Time (h)	Product (Yield %)[a]
1	**1g**	**3b**	**4a**	1.5	**6b** (40)
2	**1h**	**3b**	**4a**	1.5	**6c** (43)
3	**1l**	**3c**	**4a**	2.0	**6d** (41)
4	**1e**	**3e**	**4a**	1.0	**6e** (39)
5	**1g**	**3e**	**4a**	1.0	**6b** (40)
6	**1a**	**3f**	**4a**	2.0	**6a** (49)
7	**1h**	**DPA**	**4a**	1.5	**6c** (43)

[a] Isolated yield.

137.25, 148.28; Mass (EI) Calcd for $C_{13}H_{12}ClN$ 217.69; found 217.28.

*2.3.3. N-[(thiophen-2-yl) methyl] aniline (**3c**)*

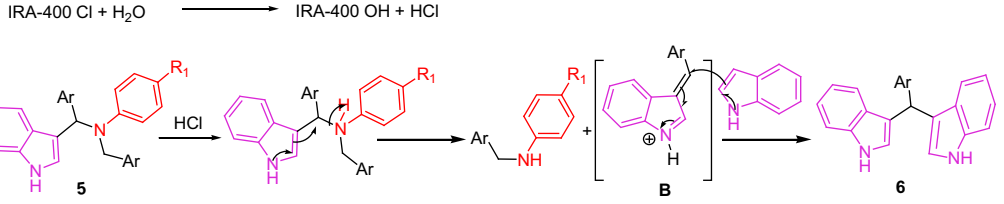
Yellow oil; Yield = 92%, FT-IR (KBr): (ν_{max}) = 3401, 3300, 1741, 1507, 1404, 1222, 1071, 962 cm^{-1}; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 3.92 (s, 1H, NH), 4.41 (s, 2H, CH_2), 6.58 (d, J = 10.0 Hz, 2H, Ar-H), 6.66 (t, J = 9.0 Hz, 1H, Ar-H), 6.86–6.88 (m, 1H, Ar-H), 6.92 (s, 1H, Ar-H), 7.08–7.12 (m, 3H, Ar-H); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 43.54, 113.45, 118.14, 124.63, 125.08, 126.91, 129.33, 143.00, 147.66.

*2.3.4. N-[(furfur-2-yl) methyl] aniline (**3d**)*

Yellow oil; Yield = 91%; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 3.96 (br s, 1H), 4.35 (s, 2H), 6.20 (s, 1H), 6.29 (s, 1H), 6.63 (d, 2H, J = 7.5 Hz), 6.75 (t, 1H, J = 7.3 Hz), 7.12–7.18 (m, 2H), 7.43 (d, 1H, J = 7.2 Hz).

*2.3.5. N-(benzyl)-4-fluoroaniline (**3e**)*

Yellow oil; Yield = 88%, ^1H NMR (300.13 MHz, $CDCl_3$): δ = 3.93 (s, 1H, NH), 4.37 (s, 2H, CH_2), 6.71–6.72 (m, 2H, Ar-H), 6.74–6.88 (m, 1H, Ar-H), 7.10–7.16 (m, 1H, Ar-H), 7.28–7.44 (m, 5H, Ar-H); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 46.44, 114.18, 116.62, 127.85, 127.95, 128.21, 137.05, 146.89, 155.32.



Scheme 6 Plausible mechanism for the formation of **6.**

*2.3.6. N-(benzyl)-4-chloroaniline (**3f**)*

Yellow oil; Yield = 94%; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.95 (s, 1H, NH), 4.59 (s, 2H, CH_2), 6.43–6.48 (m, 2H, Ar-H), 7.04–7.05 (m, 2H, Ar-H), 7.23–7.36 (m, 5H, Ar-H); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 48.15, 113.35, 122.12, 127.42, 128.29, 129.34, 129.83, 138.25, 145.28.

*2.3.7. N-(benzyl)-4-methoxyaniline (**3g**)*

Yellow oil; Yield = 92%; FT-IR (KBr): (ν_{max}) = 3375, 2997, 2948, 1832, 1513, 1461, 1406, 1295, 1265, 1239, 1180, 1119, 1076, 1037, 823, 768, 741, 705, 558, 527, 481 cm^{-1}; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.81 (s, 3H, OCH_3), 4.17 (s, 1H, NH), 4.62 (s, 2H, CH_2), 7.01–7.04 (m, 2H, Ar-H), 7.22 (t, J = 7.4 Hz, 1H, Ar-H), 7.63–7.68 (m, 5H, Ar-H), 7.74–7.79 (m, 1H, Ar-H); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 46.74, 59.43, 113.23, 117.89, 126.69, 127.88, 128.63, 129.81, 130.90, 136.72, 137.64, 148.86.

*2.4. General procedure for synthesis of compound **5a-q***

A solution of amine **3** (1.2 mmol) and an aryl aldehyde **1** (1.0 mmol) 0.5 g of anion exchange resin (Cl in form) were added in ethanol (5 mL), and stirred for 1 h at reflux condition. Then indole **4a** (1.0 mmol) was added to the reaction mixture and continued reflux until completion of the reaction (monitored by TLC), the mixture was filtered to remove resin. The resin was washed with ethanol (2 × 3 mL). The combined solvent was evaporated *in vacuo,* and the resulting residue was purified by column chromatography on silica gel (100–200 mesh) (petroleum ether/ethyl acetate = 4/1, V/V) to afford product **5**.

*2.4.1. [(1H-indoyl-3-yl)-phenyl-methyl]-N-(benzyl) aniline (**5a**)*

Pink solid, Yield = 85%, mp 142 °C; FT-IR (KBr): (ν_{max}) = 3375, 2924, 2850, 1611, 1518, 1444, 1264, 1015, 801, 750, 710, 597, 501 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 4.28 (s, 2H, CH_2), 5.55 (s, 1H, CH), 6.56–6.57 (m, 3H, Ar-H), 6.95–7.03 (m, 3H, Ar-H), 7.12–7.27 (m, 9H, Ar-H), 7.31–7.37 (m, 5H, Ar-H), 7.89 (s, 1H, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ = 48.00, 48.68, 110.96, 112.82, 119.28, 120.07, 120.63, 121.97, 123.94, 125.98, 127.14, 127.24, 127.65, 128.16, 128.95, 129.76, 133.25, 136.76, 139.57, 144.68, 146.55; Mass (EI) Calcd for $C_{28}H_{24}N_2$ 388.5036; found 388.5035.

*2.4.2. N-[(1H-indol-3-yl)-(2-methoxyphenyl)-methyl]-N-(benzyl) aniline (**5b**)*

Pink solid, Yield = 72%, mp 60 °C; FT-IR (KBr): (ν_{max}) = 3410, 3045, 2949, 2894, 2831, 1671, 1607, 1513, 1452, 1333, 1241, 1176, 1096, 1019, 812, 746, 609 cm^{-1}; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.78 (s, 3H, OCH_3), 4.29 (s, 2H, CH_2), 5.29 (s, 1H, CH), 6.02 (s, 1H, Ar-H), 6.55–6.59 (m, 3H, Ar-H), 6.84–6.92 (m, 2H, Ar-H), 6.99–7.07 (m, 4H, Ar-H), 7.14–7.20 (m, 2H, Ar-H), 7.27–7.39 (m, 7H, Ar-H), 7.84 (s, 1H, NH); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 40.26, 48.84, 55.82, 110.73, 111.03, 112.82, 119.20, 120.22, 120.41, 120.55, 121.91, 124.05, 127.19, 127.34, 127.82, 128.72, 129.88, 129.97, 133.17, 133.33, 136.86, 139.74, 146.42, 157.07; Mass (EI) Calcd for $C_{29}H_{26}N_2O$ 418.5295; found 418.5293.

*2.4.3. N-[(1H-indol-3-yl)-(4-methylphenyl)-methyl]-N-(benzyl) aniline (**5c**)*

Pink solid, Yield = 70%; mp 78–80 °C; FT-IR (KBr): (ν_{max}) = 3398, 2963, 2921, 1608, 1514, 1450, 1258, 1091, 1021, 801, 738 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 2.21 (s, 3H, CH_3), 4.17 (s, 2H, CH_2), 5.42 (s, 1H, CH), 6.44–6.46 (m, 3H, Ar-H), 6.88–7.04 (m, 7H, Ar-H), 7.12–7.25 (m, 9H, Ar-H), 7.75 (s, 1H, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ = 47.61, 48.70, 111.00, 112.85, 119.27, 120.13, 120.76, 121.95, 123.95, 127.19, 127.26, 127.46, 127.55, 127.68, 128.21, 128.84, 128.99, 129.18, 129.32, 133.55, 135.40, 136.78, 139.64, 141.74, 146.52; Mass (EI) Calcd for $C_{29}H_{26}N_2$ 402.5301; found 402.5301.

*2.4.4. N-[(1H-indol-3-yl)-(4-bromophenyl)-methyl]-N-(benzyl) aniline (**5d**)*

Pink solid, Yield = 74%, mp 62–64 °C; FT-IR (KBr): (ν_{max}) = 3415, 2924, 1608, 1512, 1325, 1258, 1071, 1004, 801, 738 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 4.28 (s, 2H, CH_2), 5.49 (s, 1H, CH), 6.54–6.57 (m, 3H, Ar-H), 6.96–6.99 (m, 3H, Ar-H), 7.07–7.37 (m, 13H, Ar-H), 7.92 (s, 1H, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ = 47.45, 48.62, 111.05, 112.86, 119.83, 119.94, 120.04, 122.14, 123.95, 126.92, 127.63, 128.17, 128.64, 128.87, 128.95, 129.69, 130.72, 131.26, 132.54, 136.77, 139.49, 143.78, 146.72; Mass (EI) Calcd for $C_{28}H_{23}BrN_2$ 467.3996; found 467.3996.

*2.4.5. N-[(1H-indol-3-yl)-(3-nitrophenyl)-methyl]-N-(benzyl) aniline (**5e**)*

Brown solid, Yield = 78%, mp 66 °C; FT-IR (KBr): (ν_{max}) = 3417, 2963, 1608, 1518, 1264, 1077, 806, 693 cm^{-1}; ^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 4.32 (s, 2H, CH_2), 5.69 (s, 1H, CH), 6.63 (d, J = 8.5 Hz, 3H, Ar-H), 7.03–7.06 (m, 3H, Ar-H), 7.20–7.25 (m, 2H, Ar-H), 7.32–7.33 (m, 1H, Ar-H), 7.37–7.45 (m, 7H, Ar-H), 7.60 (d, J = 7.5 Hz, 1H, Ar-H), 8.05 (s, 1H, NH), 8.08–8.10 (m, 1H, Ar-H), 8.14–8.15 (m, 1H, Ar-H); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 47.76, 48.54, 111.26, 113.01, 119.23, 119.61, 119.65, 121.33, 122.26, 123.78, 124.06, 126.67, 127.32, 127.61, 128.67, 129.07, 129.69, 131.48, 135.10, 136.82, 139.38, 146.99, 147.04, 148.45; Mass (EI) Calcd for $C_{28}H_{23}N_3O_2$ 433.5011; found 433.5010.

*2.4.6. N-[(1H-indol-3-yl)-(4-nitrophenyl)-methyl]-N-(benzyl) aniline (**5f**)*

Pink solid, Yield = 78%, mp 68 °C; FT-IR (KBr): (ν_{max}) = 3417, 2957, 1603, 1512, 1258, 1094, 1021, 806, 688 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 4.19 (s, 2H, CH_2), 5.54 (s, 1H, CH), 6.48 (d, J = 8.4 Hz, 3H, Ar-H), 6.89–6.93 (m, 4H, Ar-H), 7.08–7.10 (m, 2H, Ar-H), 7.15–7.29 (m, 8H, Ar-H), 7.94 (s, 1H, NH), 8.01 (d, J = 8.4 Hz, 2H, Ar-H); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ = 46.88, 47.45, 110.0, 110.20, 110.33, 111.91, 117.97, 118.58, 118.61, 118.90, 119.03, 121.32, 121.60, 122.49, 123.00, 125.61, 126.28, 126.54, 126.60, 127.17, 127.62, 128.66, 130.31, 135.72, 128.29, 145.35, 145.95, 151.47; Mass (EI) Calcd for $C_{28}H_{23}N_3O_2$ 433.5011; found 433.5015.

*2.4.7. N-[(1H-indol-3-yl)-(thiophen-2-yl)-methyl]-N-(benzyl) aniline (**5g**)*

Pink solid, Yield = 70%, mp 88–90 °C; FT-IR (KBr): (ν_{max}) = 3387, 1612, 1513, 1326, 1268, 1088, 741, 691,

504 cm^{-1}; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 4.34 (s, 2H, CH_2), 5.83 (s, 1H, CH), 6.61–6.63 (m, 2H, Ar-H), 6.81–6.84 (m, 2H, Ar-H), 6.95–6.97 (m, 1H, Ar-H), 7.05–7.08 (m, 1H, Ar-H), 7.17–7.22 (m, 4H, Ar-H), 7.29–7.34 (m, 2H, Ar-H), 7.35–7.42 (m, 6H, Ar-H), 7.95 (s, 1H, NH); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 43.23, 48.63, 111.09, 112.84, 119.87, 120.49, 122.08, 123.80, 125.32, 126.83, 127.28, 127.67, 128.66, 128.98, 129.29, 129.79, 133.19, 136.62, 139.53, 146.88, 149.33; Mass (EI) Calcd for $C_{26}H_{22}N_2S$ 394.5313; found 394.5324.

*2.4.8. N-[(1H-indol-3-yl)-(1-napthyl)-methyl]-N-(benzyl) aniline (**5h**)*

Brown solid, Yield = 72%, mp 60–62 °C; FT-IR (KBr): (ν_{max}) = 3416, 3047, 2844, 1706, 1609, 1513, 1455, 1407, 1325, 1260, 1180, 1087, 1016, 789, 742, 698, 611, 522, 478 cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 4.14 (s, 2H, CH_2), 5.12 (s, 1H, CH), 6.19-6.25 (m, 2H, Ar-H), 6.41 (d, J = 8.4 Hz, 2H, Ar-H), 6.85–6.93 (m, 3H, Ar-H), 6.99–7.05 (m, 2H, Ar-H), 7.13–7.30 (m, 10H, Ar-H, NH), 7.59 (d, J = 8.1 Hz, 2H, Ar-H), 7.73 (d, J = 7.5 Hz, 1H, Ar-H), 7.99 (d, J = 8.1 Hz, 1H, Ar-H); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 42.76, 47.58, 109.99, 117.74, 117.82, 118.22, 118.81, 119.28, 120.90, 123.39, 123.58, 124.21, 124.36, 124.80, 124.93, 125.63, 125.82, 126.00, 126.62, 127.12, 127.55, 127.88, 128.69, 128.91, 130.88, 131.73, 132.87, 135.63, 138.45, 139.26, 145.20; Mass (EI) Calcd for $C_{32}H_{26}N_2$ 438.5622; found 438.5621.

*2.4.9. N-[(1H-indol-3-yl)-phenyl)-methyl]-N-(4-(chlorobenzyl) aniline (**5i**)*

Pink solid, Yield = 78%, mp 66 °C; FT-IR (KBr): (ν_{max}) = 3412, 3049, 2854, 1706, 1605, 1513, 1453, 1409, 1321, 1274, 1181, 1088, 1004, 879, 806, 744, 701, 598, 487 cm^{-1}; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 4.29 (s, 2H, CH_2), 5.60 (s, 1H, CH), 6.56–6.59 (m, 3H, Ar-H), 7.00–7.08 (m, 3H, Ar-H), 7.17–7. 37 (m, 13H, Ar-H), 7.93 (s, 1H, NH); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 47.93, 47.98, 111.03, 112.88, 119.29, 120.06, 120.51, 122.01, 123.99, 126.04, 127.09, 128.22, 128.34, 128.75, 128.95, 129.73, 129.81, 130.29, 132.88, 133.48, 136.74, 138.14, 144.63, 146.22; Mass (EI) Calcd for $C_{28}H_{23}ClN_2$ 422.9486; found 422.9486.

*2.4.10. N-[(1H-indol-3-yl)-(4-bromophenyl)-methyl]-N-(4-chlorobenzyl) aniline (**5j**)*

Brown solid, Yield = 75%, mp 124 °C; FT-IR (KBr): (ν_{max}) = 3356, 3213, 3051, 2867, 1610, 1508, 1484, 1445, 1407, 1345, 1252, 1183, 1086, 1006, 802, 740, 613, 559, 505 cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 4.17 (s, 2H, CH_2), 5.42 (s, 1H, CH), 6.44 (d, J = 7.8 Hz, 3H, Ar-H), 6.89 (d, J = 8.1 Hz, 3H, Ar-H), 6.99–7.07 (m, 5H, Ar-H), 7.11–7.29 (m, 7H, Ar-H), 7.85 (s, 1H, NH); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 47.42, 47.87, 111.10, 112.90, 119.43, 119.93, 122.17, 123.97, 126.86, 128.77, 128.82, 129.72, 130.71, 131.29, 132.76, 132.91, 136.74, 138.05, 143.70, 146.38; Mass (EI) Calcd for $C_{28}H_{22}BrClN_2$ 501.8447; found 501.8445.

*2.4.11. N-[(1H-indol-3-yl)-(4-methoxyphenyl)-methyl]-N-[(thiophen-2-yl) methyl] aniline (**5k**)*

Pink solid, Yield = 75%, mp 50 °C; FT-IR (KBr): (ν_{max}) = 3409, 3046, 2953, 2831, 1706, 1607, 1509, 1453, 1305, 1247, 1174, 1092, 1026, 809, 744, 702, 579 cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 3.65 (s, 3H, OCH_3), 4.34 (s, 2H, CH_2), 5.41 (s, 1H, CH), 6.41 (s, 1H, Ar-H), 6.48 (d, J = 8.4 Hz, 2H, Ar-H), 6.69 (d, J = 8.7 Hz, 2H, Ar-H), 6.83–6.94 (m, 5H, Ar-H), 7.01–7.18 (m, 7H, Ar-H), 7.75 (s, 1H, NH); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 43.80, 47.18, 55.27, 111.07, 113.19, 113.63, 119.28, 120.13, 120.84, 121.98, 123.98, 124.62, 125.11, 126.89, 127.12, 129.74, 129.89, 134.17, 136.80, 136.92, 143.11, 145.98, 157.87; Mass (EI) Calcd for $C_{27}H_{24}N_2OS$ 424.5573; found 424.5601.

*2.4.12. N-[(1H-indol-3-yl)-(4-bromophenyl)-methyl]-N-[(thiophen-2-yl)-methyl] aniline (**5l**)*

Pink solid, Yield = 72%, mp 68 °C; FT-IR (KBr): (ν_{max}) = 2965, 1610, 1513, 1261, 1094, 1022, 803, 699 cm^{-1}; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 4.48 (s, 2H, CH_2), 5.53 (s, 1H, CH), 6.54 (s, 1H, Ar-H), 6.61 (d, J = 8.5 Hz, 2H, Ar-H), 6.97–7.03 (m, 6H, Ar-H), 7.11 (d, J = 8.5 Hz, 2H, Ar-H), 7.18 (t, J = 7.75 Hz, 1H, Ar-H), 7.22–7.24 (m, 2H, Ar-H), 7.33 (d, J = 8.5 Hz, 1H, Ar-H), 7.39 (d, J = 8.0 Hz, 2H, Ar-H), 7.94 (s, 1H, NH); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 43.79, 47.52, 111.19, 113.26, 113.89, 119.53, 119.95, 120.02, 122.24, 124.11, 124.75, 125.21, 126.97, 128.22, 129.33, 129.81, 130.83, 131.37, 132.03, 133.13, 136.82, 143.02, 143.78, 146.24; Mass (EI) Calcd for $C_{26}H_{21}BrN_2S$ 473.4273; found 473.4272.

*2.4.13. N-[(1H-indol-3-yl)-(1-naphthyl)-methyl]-N-[(thiophen-2-yl)-methyl] aniline (**5m**)*

Brown solid, Yield = 72%, mp 60–62 °C; FT-IR (KBr): (ν_{max}) = 3410, 3045, 2830, 1702, 1611, 1516, 1408, 1327, 1261, 1179, 1091, 1005, 814, 744, 489 cm^{-1}; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 4.40 (s, 2H, CH_2), 5.58 (s, 1H, CH), 6.49–6.55 (m, 3H, Ar-H), 6.88–6.95 (m, 5H, Ar-H), 7.08–7.17 (m, 4H, Ar-H), 7.27–7.33 (m, 2H, Ar-H), 7.48 (d, J = 9.5 Hz, 1H, Ar-H), 7.97–8.02 (m, 3H, Ar-H, NH); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 42.59, 46.69, 110.20, 112.18, 112.27, 118.11, 118.57, 120.31, 121.31, 122.72, 123.02, 123.62, 124.09, 125.58, 125.84, 128.04, 128.65, 130.94, 134.06, 135.75, 141.75, 145.38, 125.89, 147.37; Mass (EI) Calcd for $C_{26}H_{21}N_3O_2S$ 439.5288; found 439.5287.

*2.4.14. N-[(1H-indol-3-yl)-(4-methylphenyl)-methyl]-N-[(furan-2-yl)-methyl] aniline (**5n**)*

Brown solid, Yield = 75%, mp 52 °C; FT-IR (KBr): (ν_{max}) = 3412, 3044, 2863, 1693, 1610, 1512, 1454, 1322, 1256, 1183, 1092, 1009, 923, 742, 586, 496 cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 2.23 (s, 3H, CH_3), 4.19 (s, 2H, CH_2), 5.44 (s, 1H, CH), 6.13–6.14 (m, 1H, Ar-H), 6.22–6.24 (m, 1H, Ar-H), 6.46–6.54 (m, 3H, Ar-H), 6.87–7.06 (m, 7H, Ar-H), 7.06–7.21 (m, 5H, Ar-H), 7.84 (s, 1H, NH); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 19.54, 40.18, 46.05, 105.46, 108.82, 109.45, 111.60, 117.73, 118.58, 119.19, 120.42, 122.41, 125.61, 127.30, 127.38, 132.44, 133.89, 135.22, 140.39, 144.41, 151.38; Mass (EI) Calcd for $C_{27}H_{24}N_2O$ 392.4923; found 392.4923.

*2.4.15. N-[(1H-indol-3-yl)-(4-chlorophenyl)-methyl]-N-[(furan-2-yl)-methyl] aniline (**5o**)*

Pink solid, Yield = 78%, mp 60 °C; FT-IR (KBr): (ν_{max}) = 3410, 3047, 2845, 1699, 1609, 1514, 1409, 1320, 1257,

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1182, 1088, 1010, 921, 803, 741, 589, 487 cm^{-1}; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 4.29 (s, 2H, CH_2), 5.54 (s, 1H, CH), 6.23–6.24 (m, 1H, Ar-H), 6.33–6.34 (m, 1H, Ar-H), 6.54 (s, 1H, Ar-H), 6.61 (d, J = 8.5 Hz, 2H, Ar-H), 6.99–7.03 (m, 3H, Ar-H), 7.15–7.19 (m, 4H, Ar-H), 7.21–7.25 (m, 3H, Ar-H), 7.33 (d, J = 8.5 Hz, 1H, Ar-H), 7.37 (s, 1H, Ar-H), 7.93 (s, 1H, NH); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 41.70, 47.44, 107.15, 110.46, 111.18, 113.23, 119.51, 120.03, 120. 14, 122.23, 124.09, 126.96, 128.42, 129.77, 130.39, 131, 80, 133.16, 136.81, 142.06, 143.24, 146.22, 152.84; Mass (EI) Calcd for $C_{26}H_{21}ClN_2O$ 412.9107; found 412.9145.

2.4.16. N-[(1H-indol-3-yl)-(3-nitrophenyl)-methyl]-N-(benzyl) – 4-chloroaniline (**5p**)

Pink solid, Yield = 80%, mp 72 °C; FT-IR (KBr): (ν_{max}) = 3409, 2924, 1608, 1518, 1348, 1088, 806, 738 cm^{-1}; ^1H NMR (400.13 MHz, $CDCl_3$): δ = 4.19 (s, 2H, CH_2), 5.57 (s, 1H, CH), 6.46–6.49 (m, 3H, Ar-H), 6.92 (d, J = 7.2 Hz, 3H, Ar-H), 7.07–7.12 (m, 2H, Ar-H), 7.16 (s, 4H, Ar-H), 7.26–7.34 (m, 3H, Ar-H), 7.47–7.48 (m, 1H, Ar-H), 7.94–8.01 (m, 3H, Ar-H, NH); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ = 47.74, 47.82, 111.23, 113.06, 119.20, 119.62, 121.33, 122.38, 123.38, 123.76, 123.99, 126.66, 128.78, 129.06, 129.70, 131.72, 132.96, 135.06, 136.82, 137.96, 146.97, 148.46; Mass (EI) Calcd for $C_{28}H_{22}ClN_3O_2$ 467.9462; found 467.9461.

2.4.17. N-[(1H-indol-3-yl)-(2-ferrocnyl)-methyl]-N-(benzyl) -4-methoxyaniline (**5q**)

Brown solid, Yield = 72%, mp 66 °C; FT-IR (KBr): (ν_{max}) = 3408, 3006, 2894, 2831, 1609, 1512, 1456, 1413, 1300, 1248, 1172, 1098, 1029, 816, 745, 490 cm^{-1}; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 3.79 (s, 3H, OCH_3), 3.96 (s, 1H, ferrocene group), 4.02 (s, 5H, ferrocene group), 4.10 (s, 2H, ferrocene group), 4.17 (s, 1H, ferrocene group), 4.22 (s, 2H, CH_2), 5.23 (s, 1H, CH), 6.58 (d, J = 8.5 Hz, 2H, Ar-H), 6.78 (s, 1H, Ar-H), 6.86 (d, J = 8.0 Hz, 2H, Ar-H), 6.96 (t, J = 7.8 Hz, 1H, Ar-H), 7.10–7.16 (m, 3H, Ar-H), 7.25–7.29 (m, 5H, Ar-H), 7.88 (s, 1H, NH); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 41.53, 47.15, 54.26, 66.24, 67.58, 67.63, 109.85, 111.55, 112.93, 118.08, 118.87, 120.68, 121.33, 127.95, 128.43, 130.15, 132.75, 125.59, 145.43; Mass (EI) Calcd for $C_{33}H_{30}FeN_2O$ 526.4491 found 526.4490.

2.4.18. 3,3′-Bis-indolylphenylmethane (**6a**)

Pink solid, Yield = 49%, mp 124–126 °C; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 5.92 (s, 1H, CH), 6.67 (d, J = 1.5 Hz, 2H, Ar-H), 7.02–7.05 (m, 2H, Ar-H), 7.18–7.25 (m, 3H, Ar-H), 7.28–7.32 (m, 3H, Ar-H), 7.36–7.39 (m, 3H, Ar-H), 7.42 (d, J = 8.0 Hz, 2H, Ar-H), 7.91 (s, 2H, 2(NH)); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 111.05, 119.24, 119.73, 119.94, 121.92, 123.61, 126.13, 127.10, 128.22, 128.43, 128.73, 136.71, 144.02.

2.4.19. 3,3′-Bis-indolyl-(3-nitrophenyl)methane (**6b**)

Brown solid, Yield = 51%, mp 220 °C; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 6.02 (s, 1H, CH), 6.64 (s, 2H, Ar-H), 7.07 (t, J = 7.3 Hz, 2H, Ar-H), 7.24 (t, J = 7.3 Hz, 2H, Ar-H), 7.38–7.46 (m, 5H, Ar-H), 7.71 (d, J = 8.0 Hz, 1H, Ar-H), 7.96 (s, 2H, 2(NH)), 8.11 (d, J = 8.5 Hz, 1H, Ar-H), 8.25 (s, 1H, Ar-H); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 40.02, 111.36, 118.24, 119.57, 121.53, 122.33, 123.61, 123.75, 126.66, 129.18, 134.95, 136.75, 146.42, 148.49.

2.4.20. 3,3′-Bis-indolyl-(4-nitrophenyl)methane (**6c**)

Brown solid, Yield = 53%, mp 218–222 °C; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 5.99 (s, 1H, CH), 6.69 (s, 2H, Ar-H), 7.03 (t, J = 7.5 Hz, 2H, Ar-H), 7.20 (t, J = 7.5 Hz, 2H, Ar-H), 7.34 (d, J = 7.5 Hz, 2H, Ar-H), 7.39 (d, J = 8.5 Hz, 2H, Ar-H), 7.51 (d, J = 8.0 Hz, 2H, Ar-H), 8.02 (s, 2H, 2(NH)), 8.15 (d, J = 9.0 Hz, 2H, Ar-H).

2.4.21. 3,3′-Bis-indolyl-(ferrocenyl) methane (**6d**)

Brown solid, Yield = 41%, mp 200 °C; ^1H NMR (500.13 MHz, $CDCl_3$/DMSO-d_6): δ = 3.88 (s, 5H, ferrocene group), 4.01 (s, 2H, ferrocene group), 4.15 (s, 2H, ferrocene group), 5.57 (s, 1H, CH), 6.84–7.00 (m, 6H, Ar-H), 7.22–7.26 (m, 2H, Ar-H), 7.41 (d, J = 9.0 Hz, 2H, Ar-H), 8.89 (br, s, 2H, 2(NH)); ^{13}C NMR (125.77 MHz, $CDCl_3$/DMSO-d_6): δ = 33.43, 65.92, 67.57, 92.46, 110.16, 117.62, 118.65, 119.39, 120.22, 121.49, 126.07, 135.45.

2.4.22. 3,3′-Bis-indolyl-(4-chlorophenyl) methane (**6e**)

Pink solid, Yield = 45%, mp 76 °C; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 5.89 (s, 1H, CH), 6.64–6.66 (m, 2H, Ar-H), 7.03–7.07 (m, 2H, Ar-H), 7.19–7.23 (m, 2H, Ar-H), 7.26–7.31 (m, 4H, Ar-H), 7.36–7.40 (m, 4H, Ar-H), 7.92 (s, 2H, 2 (NH)); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 39.64, 111.04, 111.13, 119.21, 119.25, 119.38, 119.74, 119.83, 119.95, 121.94, 122.09, 123.61, 126.91, 128.23, 128.38, 128.74, 130.09, 131.81, 136.72, 142.59.

3. Results and discussion

Initially, we studied the DRA reaction of benzaldehyde **1a** (2 mmol) and aniline **2a** (2.2 mmol) as model substrates in methanol in the presence of Amberlite IRA-400 Cl (0.5 g) resin as a catalyst. The reaction afforded an imine that without further purification was then exposed to $NaBH_4$ (2 mmol) affording *N*-benzyl aniline **3a** in 98% yield. The scope of the reaction was explored using a number of different aldehydes (**1a,e,i,j**) and aryl amines (**2a-d**) to afford amine products **3a–g** in excellent yields ((Scheme 1, Table 1, entries 1–7).

The role of Amberlite IRA-400 Cl resin in the reaction has been found to be essential. A blank experiment without IRA-400 Cl resin, reductive amination reaction with $NaBH_4$ did not proceed but afforded only the carbonyl reduction product (Scheme 2, Table 1-entry 8).

In order to demonstrate the synthetic use of the secondary amine **3a** thus formed, amine **3a** was subjected to a MCR with benzaldehyde **1a** and indole **4a** without any catalyst under neat conditions (Scheme 3, Table 2, entry 1). The reaction afforded *N*-((1*H*-indol-3-yl) (phenyl methyl)-*N*-benzyl aniline **5a** and bis-indole **6a,** in 25% and 45% yields, respectively. The identity of compounds **5a** and **6a** was established from spectroscopic data (see Supplementary Information). To optimize the synthesis of **5a**, parameters such as solvent, resin type and reaction times were considered. Thus, a reaction of *N*-benzyl aniline **3a** (1.2 mmol), benzaldehyde **1a** (1.0 mmol) and indole **4a** (1.0 mmol) in the presence of commercial

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Amberlite IR-120 resin (0.5 g) catalyst in ethanol afforded bis indolyl **6a** in 45% yield along with 10% yield of **5a** (Table 2, entry 2). The same reaction was carried out with Amberlite IRA-400 Cl (0.5 g) in MeOH afforded **5a** in 65% yield along with 15% yield of **6a** (Table 2, entry 3). To study the role of the solvent, the reaction was carried out in EtOH, CH_3CN, $(CH_2Cl)_2$, and toluene (Table 2, entries 4–7). The results show that when using toluene only a trace amount of compound **5a** was isolated (Table 2, entry 6). On the other hand, a better yield of compound **5a** was observed when using CH_3CN, and 1,2-dichloroethane (Table 2, entry 4 and 5). To reduce the formation of by-product **6a** and increase the yield of **5a**, the reaction was carried out using Amberlite IRA-400 Cl resin (0.5 g) in EtOH and obtained **5a** in 85% yield in 3 h (Table 2, entry 7). These results showed that the Amberlite IRA-400 Cl resin has a remarkable effect in suppressing the formation of the by-product and driving the selective formation of **5a**. It was also noted that the best catalytic activity of Amberlite IRA-400 Cl resin was optimized to be 0.5 g (Table 2, entry 7) and any excess catalyst, beyond this proportion (0.5 g), did not show further increase in the conversion and yield of the product (Table 2, entry 8) while decreasing the amount of catalyst from 0.5 to 0.4 g lowered the substrate conversion rate (Table 2, entry 9).

The recyclability of the Amberlite IRA-400 Cl resin catalyst has been studied and the results are shown in Table 3. However, the catalyst can be regenerated and used for reactions with no loss of yield [32]. The regeneration of catalyst can be done by washing the filtered resin with ethanol and then conditioned in a column with 10% potassium chloride solution. The resulted resin is washed with distilled water until the washing was free from chloride. The resins were then air dried and can be used for further studies [32].

In order to demonstrate the scope of the reaction, under optimized condition, the methodology was extended with various aryl aldehydes **1a–l**, aryl amines **3a–g** and indole **4** have been carried out (Table 4). The reactions provided a number of [(1*H*-indoyl-3-yl)-phenyl-methyl]-*N*-benzyl aniline derivatives **5b–q** in very good yield (Table 4, entries 1–17). The conversion was completed within 1.5–3.0 h and the products **5b–q** were formed in high yields (Table 4). The 3- and 4-nitrobenzaldehyde **1g–h** (Table 4, entries 5–6) underwent a three-component reaction to afford the products **5e** and **5f** in 78% yields. The chloro and bromo benzaldehyde **1e** and **f** were also compatible substrates for the MCR (Table 4, entries 4, 10, 12, and 15). In the case of 4-methylbenzaldehyde **1h** (Table 4, entry 3) the product yield was slightly decreased (70%), while 2-methoxy benzaldehyde **1b** also reacted gave **5b** in 72% yield (Table 4, entry 2). In addition, 1-naphthaldehyde **1k** also gave the good yield of **5h** in 72% yield (Table 4, entry 8). It is noteworthy that heteroaryl and organometallic aldehydes such as 2-thiophenealdehyde **1i** and ferrocenealdehyde **1l** also participated in the reaction afforded 3-amino-alkylated products **5g** and **5q**, respectively (Table 4, entries 7 and 17). To diversify this reaction, the *N*-benzyl aniline has been replaced with *N*-substituted amines **3b–d,f,g**. Thus, the three component reaction with substituted aldehyde and indole **4** under optimized reaction conditions provided the desired products **5i–q** in good yields (Chart 1, Table 4, entries 9–17). The Amberlite IRA-400 Cl can be reused for three times with a slight decrease in the yield. All the new compounds were characterized by spectroscopic data such as FT-IR, ^{1}H NMR, ^{13}C NMR, and ESI-Mass spectra.

It should be noted that when the reactions were carried out with of *N*-substituted anilines **3b,e,f** (substitutions at para position with electron withdrawing group such as fluoro and chloro), diphenylamine, aldehyde and indole afforded only bis indole products **6a–e** as the main products and quantitative unreacted *N*-substituted anilines **3b,e,f** and diphenylamine. The expected compound **5** were not observed (Scheme 4, Chart 1, Table 5, entries 1–7). The reactivity difference is due to highly electron withdrawing group present in the anilines.

A plausible mechanism for the formation of 3-substituted indole derivative **5** and bis-indole **6** is shown in Schemes 5 and 6. Initially, in the presence of Amberlite IRA-400 Cl resin, the iminium ion intermediate **A** is generated *in situ* from the aldehyde **1** and aromatic amine **3** by the elimination of a water molecule. A subsequent nucleophilic attack of indole **4** to intermediate **A** affords the product **5** as shown in Scheme 5.

Subsequently, the HCl generated from the Amberlite IRA-400 Cl resin and moisture triggers the elimination of a secondary amine from compound **5** to form intermediate **B**. A subsequent reaction with indole **4** with intermediate **B** affords bis-indole **6** (Scheme 6).

4. Conclusion

In summary, a facile and efficient synthesis of 3-aminoalkylated indole and bis-indole derivatives *via* an MCR catalyzed by Amberlite IRA-400 Cl resin has been demonstrated. A plausible mechanism for the formation of 3-aminoalkylated indoles is proposed. This method is of great value due to efficiency and easy handling of the catalyst.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jscs.2016.01.009.

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